REMARKS/ARGUMENTS

The Advisory Action mailed October 27, 2005 states

> The Applicant has not provided any working examples in the instant specification to show how a seven-carbon fatty acid can treat a cardiac disorder such as atherosclerosis. Applicant's working examples are limited to an in-vitro cell assay of cells derived from a deceased infant (how can this experiment provide results to administering the said compounds in-vivo to a patient suffering from cardiomyopathy). Furthermore, no working examples on how to exemplify a method for directly providing fuel to the heart tissue of a patient.

The Action's characterizations are inoperative. The specification clearly provides in Example 2, the treatment of a human infant with triheptanoin (a seven carbon fatty acid) to treat neonatal translocase deficiency (a cardiac disorder) (See, Paragraph [0089]). The specification clearly states as quoted below that the infant was delivered, treated and discharged at 7-8 weeks. The infant continued to grow and thrive at four and a half months. The specification DOES NOT state the infant was or is deceased at the time of treatment! More specifically:

> [0090] At 38 weeks gestation, **delivery of the infant whose amniocytes tested positive for severe translocase deficiency** as described in Example 1 was accomplished. Cord blood was analyzed for total and free carnitine levels as well as levels of individual acylcarnitines by tandem mass spectrometry. (Yang, et al. 1998. "Identification of four novel mutations in patients with carnitine palmitoyltransferase II (CPT II) deficiency," Mol Genet Metab 64:229-236). Maternal blood at the time of delivery was also assayed for these same levels. Results confirmed that the infant suffered from severe translocase deficiency. (emphasis added).

> [0091] **Within the first twelve hours after delivery, a low fat formula supplemented with triheptanoin was fed to the infant via a nasogastric tube.** Subsequent feedings with the triheptanoin-supplemented formula were given at the same frequency as any full-term infant. Supplements of carnitine, biotin, and cyanocobalamin were not required. (emphasis added).

> [0093] **The intervention of triheptanoin-supplemented formula was a total success in suppressing the effects of translocase deficiency.** During the infant's hospital stay, the various physiological parameters given above were reported within normal ranges. The **infant was discharged from the hospital at 7-8 weeks of age exhibiting perfect dietary management** with the triheptanoin-supplemented formula. During continued maintenance on the triheptanoin-supplemented formula, **the infant has maintained an average weight gain per day of 35 grams per day, compared to the average weight gain of 20-25 grams per day for the average formula-fed infant. At four and a half months of age, the infant continued to thrive on the triheptanoin-supplemented formula,** and no carnitine, biotin, or vitamin B12 supplements had been required. (emphasis added).

In fact, the example in the specifications shows a treatment with a seven carbon fatty acid for neonatal translocase deficiency (which results in cardiac hypertrophy, hypoglycemia, hyperammonemia and death as result of cardiomyopathy complications). The Example clearly showed a method of treatment including the method of administer (e.g., [0091]). In fact the infant in Example 2 maintained an average weight gain per day of 35 grams per day, compared to the average weight gain of 20-25.

The art knows that severe translocase deficiency or severe carnitine/acylcarnitine translocase (CACT) deficiency result in weakness, cardiac hypertrophy, hypoglycemia, hyperammonemia and death as result of cardiomyopathy complications.[1] In sharp contrast, the present invention "...was a total success in suppressing the effects of translocase deficiency." (paragraph [0093]).

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[1] Chalmers, R.A., Stanley, C.A., English, N. and Wigglesworth, J.S. Mitochondrial carnitine-acylcarnitine translocase deficiency presenting as sudden neonatal death. J Pediatrics 131:220, 1997.

Morris, A.A.M., Olpin, S.E., Brivet, M., et al. A patient with carnitine-acylcarnitine translocase deficiency with a mild phenotype. J Pediatrics 132:514, 1998.

Ogier de Baulney, H., Slama, A., Touati, G., et al. Neonatal hyperammonemia caused by a defect of carnitine-acylcarnitine translocase. J Pediatrics 127:723, 1995

Roe, C.R. and Ding, J. Mitochondrial Fatty Acid Oxidation Disorders. In, The Metabolic and Molecular Basis of Inherited Disease. 8th Edition, 2001. Scriver, Beaudet, et al. McGraw-Hill. Chapter 101, pg. 2297-2326.

REMARKS/ARGUMENTS

Claims 17-52 are pending in this Application. The final Office Action mailed on June 2, 2005, includes the following rejections:

1. Claims 17-52 are rejected under 35 U.S.C. § 112 first paragraph.

Applicant respectfully addresses the basis for each of the Examiner's rejections below.

Claim Rejections – Claims 17-52 are rejected under 35 U.S.C. 112 first paragraph as failing to comply with the enablement requirement.

The Action rejects claims 17-52 under 35 U.S.C. § 112 first paragraph, which states:

> The claims contain subject matter which was not described in the Specification in such a way as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant respectfully submits that the specification is enabled to support claims 17-52 and fully complies with 35 U.S.C. § 112 first paragraph. For example, the specification provides detailed examples using a seven carbon fatty acid and states that substituted, unsaturated or branched heptanoates can be used in addition to other modified seven-carbon fatty acids ([0070]). The present specification also provides considerable direction and guidance on how to practice the claimed invention and presents working examples and all of the methods needed to practice the invention were either well known in the art or disclosed in the specification (e.g., See, *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)).

Furthermore, the study of fatty acids has been around for decades; and as such, much is known in the art regarding there properties, reactions and modification. Therefore, it is not necessary for the specification to provide every modification and configuration, See, e.g., *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991) (Furthermore, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted). All that is necessary is that one skilled in the art be able to practice the claimed

invention, given the level of knowledge and skill in the art. Further, the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The Applicant asserts that the specification as disclosed is enabled to support claims 17-52 and complies with 35 U.S.C. § 112 first paragraph and does not require undue experimentation. Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Applicant asserts that when the factors to determine undue experimentation set forth in *In re Wands* are addressed, the claimed invention is enabled so that any person minimally skilled in the art can make and use the invention without undue experimentation. Applicant addresses the relevant *In re Wands* factors in turn.

With regards to the nature of the invention, state of the prior art, relative skill of those in the art and predictability of the art. As mentioned above, the study of fatty acids has been around for decades; and as such, much is known in the art regarding there properties, reactions and modification. For example, certain synthetic odd-carbon number triglycerides have been tested for use in food products as potential fatty acid sources and in the manufacture of food products. The oxidation rates of odd-chain fatty acids from C_7 and C_9 triglycerides have been examined in vitro in isolated piglet hepatocytes. e.g., *Odle, et al.* 1991. "Utilization of medium-chain triglycerides by neonatal piglets: chain length of even- and odd-carbon fatty acids and apparent digestion/absorption and hepatic metabolism," *J Nutr* 121:605-614; *Lin, X, et al.* 1996. (see [0009]). Therefore, given the nature of the invention, the extensive material contained in the prior art, those of skill in the art are not necessarily PhDs, MS and MDs but also pharamacists and compounders of pharmaceuticals provide a wide range of level of skill in the art and the predictability of decades of the fatty acid chemistry and fatty acid metabolism, these factors clearly indicate any person skilled in the art can make and use the invention without undue

experimentation given the considerable direction and guidance supplied by the present specification.

With reference to the breadth of the claims, the claims are not overly broad as the specification teaches the use of a select group of fatty acids (e.g., to seven carbon fatty acids) as opposed to all fatty acids or different groups containing fatty acids of vastly different numbers of carbons. For example, the seven carbon fatty acids are a group of fatty acids with similar chemical properties as a group, e.g., found mainly in milk fats, have similar physical properties and interactions and so forth. Although, the fatty acid may be modified, such modifications are well known to persons of ordinary skill in the art. Additionally, the specification provides examples of disorders that may be treated with the present invention. Upon reading the specification, the skilled artisan will know of other disorders that may be treated. Furthermore, it is not necessary for the specification to provide every modification, configuration or disorder, See, e.g., *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). The specification and the knowledge of the skilled artisan clearly enables the full scope of the claimed invention without undue experimentation.

With regards to the amount of direction or guidance provided and the presence or absence of working examples. The specification provides examples in the form of well-known characteristics and generally accepted *in vitro* systems, e.g., cell culture examples using human cells and an *in vivo* example of treating a living infant (see e.g., [0089]). In addition to the examples in the specification, claim 26 provides one embodiment of a dosage amount and claims 43-46 provide embodiments for different delivery methods. Therefore, all of the methods needed to practice the invention were either well known in the art or disclosed in the specification.

It is taught by the present inventor that the major sources of fuel for the heart is fatty acids and because it has the property of being gluconeogenic, triheptanoin can be used in direct fueling of heart tissue in adults recuperating from cardiac or other high-risk surgery. (See Figure 2 and [0071]). Given this fact and the knowledge of the skilled artisan, it is not necessary to provide multiple examples of directly fueling the heart, as it is inherent. Furthermore, the limited

number of available living pacients with such a condition limits the availability of primary culture cells.

The specification does provides guidance as to compounds may be used in the present invention. See, *In re Herschler*, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979) (disclosure of corticosteroid in DMSO sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO because "use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. Occasionally, a functional recitation of those known compounds in the specification may be sufficient as that description."). As is the case here, the functional recitation of those known compounds in the specification are sufficient to enable a person skilled in the art can make and use the invention without undue experimentation given the considerable direction and guidance supplied by the present specification..

With regard to the quantity of experimentation necessary, the present invention does not require difficult or time-consuming assays and all necessary information is present in the specifications or known to a person of skill in the art, for example, the skilled artisan. The specifications provide direction and guidance including examples and results. As mentioned prior, the state of the art is high as fatty acids has been studied for many decades and therefore the predictability of the art with regards to modifications and fatty acid characteristics is also quite high. Currently, those of skill in the art are PhDs, MS, MDs, pharmacists and compounders create a wide level of skill of those in the art. When these factors are taken as a whole it is clear that undue experimentation is not necessary; and thus, the specification is enabled to support claims 17-52.

As such, the specification satisfies the written description requirement under 35 U.S.C. § 112, first paragraph. For the reasons mentioned above, the Applicant respectfully requests the Examiner withdraw the rejection under 35 U.S.C. § 112.

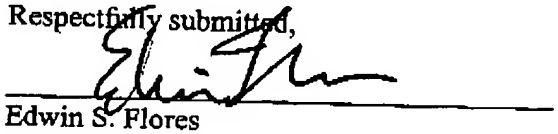
Conclusion

In light of the remarks and arguments presented above, Applicant respectfully submits that the claims in the Application are in condition for allowance. Favorable consideration and allowance of the pending Claims 17-52 are therefore respectfully requested.

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: November 2, 2005.

Respectfully submitted,



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